REMARKS

Applicants thank the Examiner for her review of the instant application. Claims 1-5 remain present for examination. For the reasons stated below, the rejections of the presently pending claims are respectfully traversed.

Rejection Under 35 U.S.C. §102

The Examiner maintains the rejection of Claims 1-5 under 35 U.S.C. §102(a) as allegedly being anticipated by Barnes (WO 00/18904, published April 6, 2000). According to the Examiner, the cited reference teaches murine TANGO 215 that is 91.3% identical to SEQ ID NO:38. The Examiner asserts that the reference also teaches antibodies that bind the polypeptide.

Applicants respectfully traverse.

Applicants have argued that (1) under the doctrine established in *In re Moore* and *Stempel*, Barnes cannot serve as prior art for the present application, and (2) Barnes neither expressly nor inherently anticipates the claims.

Barnes is not Prior Art According to the Doctrine Established under *In re Moore* and *Stempel*

Applicants submit that Applicants have shown possession of as much of the claimed invention as allegedly disclosed in the cited reference prior to its publication, and, thus, under the doctrine established in *In re Moore* and *Stempel*, Barnes cannot serve as prior art for the present application. Applicants have previously submitted a provisional patent application, filed with the PTO, serving as clear evidence of Applicants' prior possession in accordance with *In re Moore* and *Stempel*. In reply to Applicants assertions regarding *In re Moore* and *Stempel* and the accompanying evidence, the Examiner states:

> While the document can be used as evidence, Applicants again err in insisting that the argued reference, and not properly attested under 37 C.F.R. 1.131 by the inventors is sufficient to drop the rejection under 102(a). Applicant is directed to MPEP 2132.01 37 CFR 1.131 AFFIDAVIT CAN BE USED TO OVERCOME A 35 U.S.C. 102(a) REJECTION. *Office Action* at page 3.

Thus, the PTO takes the position that evidence alone, absent an accompanying Declaration under 37 C.F.R. §1.131, cannot be sufficient to antedate a reference and thereby

overcome a rejection under 35 U.S.C. §102(a). However, the fact that a Declaration under 37 C.F.R. §1.131 can serve as evidence sufficient to overcome a rejection under 35 U.S.C. §102(a), does not establish that such is the only evidence sufficient to overcome a rejection under 35 U.S.C. §102(a). Neither the M.P.E.P. nor 37 C.F.R. takes such a position. In fact, the M.P.E.P. explicitly provides at least one other form of evidence sufficient to antedate a reference in overcoming a rejection under 35 U.S.C. §102(a). *See M.P.E.P. §715.07(b).* In the present Action, the PTO provides no basis for asserting that, contrary to at least one section of the M.P.E.P., the only evidence sufficient to antedate a reference in overcoming a rejection under 35 U.S.C. §102(a) is a Declaration under 37 C.F.R. §1.131. In particular, in the present Action, the PTO provides no basis that evidence alone, absent an accompanying Declaration under 37 C.F.R. §1.131, cannot be sufficient to antedate a reference and thereby overcome a rejection under 35 U.S.C. §102(a). In contrast, the M.P.E.P. clearly admonishes the PTO to consider all evidence in evaluating the patentability of the claims. *See, e.g., M.P.E.P. §706.* The PTO has failed to consider the provisional application previously submitted by Applicants, and, thus, examination of the claims in the present Office Action is incomplete.

Notwithstanding the above, in order to facilitate prosecution of the present application, Applicants submit herewith a Declaration under 37 C.F.R. §1.131, enclosed herewith as Exhibit 1. This Declaration attests that, prior to the publication by Barnes on April 6, 2000, one or more inventors possessed the polypeptide of SEQ ID NO:38 and contemplated antibodies to the polypeptide of SEQ ID NO:38, as is demonstrated in U.S. Provisional Application 60/096,959, filed August 18, 1998. The Declaration confirms that U.S. Provisional Application 60/096,959 shows the complete nucleotide sequence of the PRO1344 nucleic acid as SEQ ID NO: 1, as well as the complete amino acid sequence of the PRO1344 polypeptide as SEQ ID NO: 2, as shown in Figures 1 and 2, respectively. The Declaration states that U.S. Provisional Application 60/096,959 also discloses antibodies that bind the PRO1344 polypeptide, including humanized antibodies and monoclonal antibodies, as shown at page 5, lines 8-9; page 27, line 13 through page 33, line 19; Example 7; and Claims 28-30. The Declaration thus concludes that the provisional application demonstrates that, no later than August 18, 1998, the inventors were in possession of as much of the claimed invention as the PTO asserts is disclosed in Barnes.

Therefore, the Declaration establishes that the provisional application clearly demonstrates possession of the invention by Applicants by at least its August 18, 1998 filing date, which is prior to the effective date of the cited reference, April 6, 2000. Accordingly, in accordance with the doctrine established under *In re Moore* and *Stempel* discussed below, Barnes cannot serve as prior art for the present application.

The well-established "Stempel Doctrine" stands for the proposition that a patent applicant can effectively swear back of and remove a cited prior art reference by showing that he or she made that portion of the claimed invention that is disclosed in the prior art reference. (*In re Stempel*, 113 USPQ 77 (CCPA 1957)). In other words, a patent applicant need not demonstrate that he or she made the entire claimed invention in order to remove a cited prior art reference. He or she need only demonstrate prior possession of that portion of his or her claimed invention that is disclosed in the prior art reference and nothing more.

The Stempel Doctrine was extended to cases where a reference disclosed the claimed compound but failed to disclose a sufficient utility for it in *In re Moore*, 170 U.S.P.Q. 260 (CCPA 1971). More specifically, the patent applicant (Moore) claimed a specific chemical compound called PFDC. In support of a rejection of the claim under 35 U.S.C. § 102, the Examiner cited a reference which disclosed the claimed PFDC compound, but did not disclose a utility for that compound. Applicant Moore filed a declaration under 37 C.F.R. § 1.131 demonstrating that he had made the PFDC compound before the effective date of the cited prior art reference, even though he had not yet established a utility for that compound. The lower court found the 131 declaration ineffective to swear back of and remove the cited reference, reasoning that since Moore had not established a utility for the PFDC compound prior to the effective date of the cited prior art reference, he had not yet completed his "invention."

On appeal, however, the CCPA reversed the lower court decision and indicated that the 131 declaration filed by Moore was sufficient to remove the cited reference. The CCPA relied on the established Stempel Doctrine to support its decision, stating:

> An applicant need **not** be required to show [in a declaration under 37 C.F.R. § 1.131] any more acts with regard to the subject matter claimed that can be carried out by one of ordinary skill in the pertinent art following the description contained in the reference....the determination of a practical utility when one is not obvious need **not** have been accomplished prior to the date of a reference

> unless the reference also teaches how to use the compound it describes. (Id. at 267, emphasis added).

Thus, *In re Moore* confirms the Stempel Doctrine, holding that in order to effectively remove a cited reference with a declaration under 37 C.F.R. § 1.131, an applicant need only show that portion of his or her claimed invention that appears in the cited reference. Moreover, *In re Moore* stands for the proposition that when a cited reference discloses a claimed chemical compound either absent a utility or with a utility that is different from the one appearing in the claims at issue, a patent applicant can effectively swear back of that reference by simply showing prior possession of the claimed chemical compound. In other words, under this scenario, the patent applicant need not demonstrate that he or she had discovered a patentable utility for the claimed chemical compound prior to the effective date of the prior art reference.

Applicants have submitted a Declaration under Rule 131 demonstrating that Applicants' U.S. Provisional Application 60/096959, filed August 18, 1998, confirms Applicants' possession prior to publication of the cited reference. Barnes' disclosure provides nothing beyond which Applicants possessed. Accordingly, in accordance with the doctrine established under *In re Moore* and *Stempel*, Barnes cannot serve as prior art for the present application.

Barnes does not Expressly or Inherently Disclose Applicants' Claims

Even if Barnes were properly prior art, which it is not, Barnes cannot anticipate Applicants' claims because no disclosure of Barnes expressly or inherently discloses Applicants' claimed antibodies.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987). The pending claims recite an isolated antibody or fragment thereof that specifically binds to the polypeptide of SEQ ID NO:38. The cited reference does not expressly disclose an antibody which specifically binds to the polypeptide of SEQ ID NO:38, and the Examiner has not established that the cited reference inherently discloses an antibody that satisfies the claims. The M.P.E.P. states that:

> To establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is **necessarily** present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency,

> however, **may not be established by probabilities or possibilities**. The mere fact that a certain thing **may** result from a given set of circumstances **is not sufficient**." *M.P.E.P.* §2112 ¶IV (8th ed. 2004), quoting *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (emphasis added).

Thus, the M.P.E.P. and cited case law makes clear that only if an antibody to the proteins disclosed in the cited references necessarily specifically binds to the polypeptide of SEQ ID NO:38 can it be said to render the claimed subject matter anticipated.

The PTO responds by stating:

> Applicants argue that the antibodies of the prior art do not expressly or inherently disclose the claimed invention because the sequences of the polypeptide are not 100% identical and any differences can change antibody binding. This is again not persuasive. The polypeptides have extensive regions of 100% identity. Antibodies made against the whole polypeptide would necessarily bind the regions of identity. The smallest region that an antibody binds is 6 consecutive amino acids (Harlow et al). *Office Action* of December 13, 2007, at page 3 (emphasis added).

Thus, the PTO appears to take the position that when two polypeptides have "extensive regions" of 100% identity, these two polypeptides necessarily have identical antibody binding properties. That is, when two polypeptides have "extensive regions" of 100% identity, there can never be an instance when a particular antibody binds only one of the two polypeptides.

This position is wholly inconsistent with the position previously taken by the PTO regarding antibodies directed to the same amino acid sequence as that recited in the present claims: "Lederman et al. disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document) and Li et al. disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document)." *Office Action dated December 26, 2006, in Appl. No. 10/063,545* at page 6. Thus, relying on Lederman and Li, the PTO has previously taken the position that even a single amino acid substitution between two polypeptides can result in differential antibody binding properties. This previous position taken by the PTO is completely dissonant with the present position taken by the PTO. Clarification is respectfully requested. For purposes of facilitating full consideration and evaluation of this cited Office Action, and the Lederman and Li references cited therein, these documents are submitted herewith as Exhibits 2-4.

In their earlier response, Applicants have pointed to the PTO's previous position that even a single amino acid substitution between two polypeptides can result in differential antibody binding properties. Applicants have requested that this position be affirmed by the PTO. In response, the PTO in the present action states:

> Applicants argue facts not relied upon by the examiner. The relied upon facts are set forth again. The examiner will not affirm facts not relied upon to make the rejection, nor references to rejections not made in this application. *Office Action* of December 13, 2007, at page 5.

Thus, the PTO refuses to consider facts other than those relied upon by the PTO in issuing the present rejection. That is, the PTO refuses to consider all facts of record, and will only consider facts relied on by the PTO in rejecting the claims. The M.P.E.P. clearly admonishes the PTO to consider all evidence in evaluating the patentability of the claims. *See, e.g., M.P.E.P. §706.* The PTO asserts that it refuses to consider facts not relied upon to reject the claims, and, thus, examination of the claims in the present Office Action is incomplete.

The PTO instead relies on references by Bendayan (J. Histochem. Cytochem. 43:881-886 (1995)), Bost *et al.* (Immunol. Invest. 17:577-586 (1988)), and Berg (U.S. Pat. No. 6,210,670), as teaching that some antibodies "cross-react" with more than one protein. These references generally teach that, on occasion, an antibody can bind more than one polypeptide (see, *e.g.*, Berg at column 3, lines 28-30, "The invention provides monoclonal antibodies that have a binding site that specifically binds to P-selectin and to E-selectin."). However, none of these references support the PTO's assertion that "[t]he polypeptides have extensive regions of 100% identity. Antibodies made against the whole polypeptide would necessarily bind the regions of identity." In fact, these references show that although some antibodies bind two polypeptides, other antibodies bind only the one of the two polypeptides, but not the other. For example, Berg at Example 2 provides three antibodies that bind both to P-selectin and to E-selectin, two antibodies that bind to E-selectin but not to P-selectin, and one antibody that binds to P-selectin but not to E-selectin. *See Berg* at column 21, lines 38-46. Thus, Berg clearly demonstrates that even though some antibodies can bind two polypeptides, not all antibodies necessarily bind the regions of identity between the two polypeptides. Accordingly, Berg demonstrates that antibodies made against related polypeptides do not necessarily bind the regions of identity. As such, the PTO's

evidence itself clearly demonstrates that the PTO's assertions on inherent antibody properties are incorrect.

Moreover, the teachings of Lederman and Li, and the PTO's previous characterizations thereof, are more relevant to the issue of inherent anticipation of the present claims. According to the PTO's previous statements, "Lederman et al. disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document) and Li et al. disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document)." Nothing in Bendayan, Bost and Berg are contrary to the PTO's previous characterizations of Lederman and Li. In particular, nothing in Bendayan, Bost and Berg demonstrates that when two polypeptides share homologous regions, "[a]ntibodies made against the whole polypeptide would necessarily bind the regions of identity." In contrast, Lederman and Li demonstrate that a single amino acid difference between polypeptides can result in elimination of antibody binding of one polypeptide, but not the other polypeptide. As such, Lederman and Li serve as evidence that when two polypeptides share homologous regions, antibodies that bind one polypeptide do not necessarily bind the other polypeptide.

Given the above, the Barnes reference can inherently anticipate the claimed invention **only if** the answer to the following question is "yes":

> 1. Does an antibody raised against the TANGO 215 protein of Barnes necessarily, always and without exception, possess the property of specifically binding to the polypeptide of SEQ ID NO:38?

This inquiry can be rephrased, such that Barnes inherently anticipates the claimed invention **only if** the answer to the following question is "yes":

> 2. Does the extrinsic evidence make it clear that there is a 100% probability that an antibody raised against the protein of Barnes possess the property of specifically binding to the polypeptide of SEQ ID NO:38?

As is clear from the above discussion and the totality of the evidence of record, the answer to both questions clearly is "no."

Barnes' TANGO 215 protein differs in amino acid sequence from Applicants' SEQ ID NO:38. The Examiner confirms this by asserting that Applicants' SEQ ID NO:38 shares 91.3% sequence identity with Barnes' TANGO 215 protein. Thus, according to the Examiner, Barnes' TANGO 215 protein differs from Applicants' SEQ ID NO:38 at over 60 amino acid locations.

The evidence of record demonstrates that an antibody that binds a first protein can fail to bind a second protein that differs from the first by only one amino acid. Since (1) Barnes' TANGO 215 protein differs from Applicants' SEQ ID NO:38 at over 60 amino acid locations, and (2) there is relevant evidence demonstrating that a single amino acid substitution in a common allele can ablate binding of a monoclonal antibody, then it follows that an antibody that binds to Barnes' TANGO 215 protein does not necessarily and always bind to Applicants' SEQ ID NO:38.

Applicants have asserted no more than the PTO has asserted: a single amino acid difference between two proteins is sufficient to destroy binding of an antibody to the protein. Applicants have relied on the PTO's references by Lederman and Li as evidence to support this statement, and there is no evidence of record contrary to Lederman and Li and the PTO's characterization thereof – *i.e.*, there is no evidence of record that an antibody raised against Barnes' TANGO 215 protein will necessarily possess the property of specifically binding to the polypeptide of SEQ ID NO:38. Given the evidence of record in the publications by Li and Lederman, and the lack of any evidence to the contrary, there exists some possibility that an antibody raised against Barnes' TANGO 215 protein will not possess the property of specifically binding to the polypeptide of SEQ ID NO:38. Because the possibility is less than 100%, one cannot answer the first question above in the affirmative: an antibody raised against the TANGO 215 protein of Barnes does not necessarily, always and without exception, possess the property of specifically binding the polypeptide of SEQ ID NO:38.

While it may be probable, indeed likely, that an antibody to Barnes' TANGO 215 protein would bind the polypeptide of SEQ ID NO:38, it is not a certainty. Mere possibility, no matter how likely, is not sufficient for inherent anticipation: "Inherency, however, **may not be established by probabilities or possibilities**. The mere fact that a certain thing **may** result from a given set of circumstances **is not sufficient**." *M.P.E.P.* §2112 ¶IV (8th ed. 2004), quoting *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (emphasis added).

In conclusion, the evidence of record makes clear that Applicants' claims are novel over Barnes because Barnes is not prior art to Applicants' claims and because Barnes does not expressly or inherently disclose Applicants' claimed invention. The Examiner provides no

factual basis to conclude otherwise. In view of the above, Applicants respectfully request removal of this rejection of the claims.

CONCLUSION

In view of the above, Applicants respectfully maintain that claims are patentable and request that they be passed to issue. Applicants invite the Examiner to call the undersigned if any remaining issues may be resolved by telephone.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 14-Apr-08

By: _____

Kerry Taylor
Registration No. 43,947
Attorney of Record
Customer No. 30,313
(619) 235-8550

4989872
031008